

Amendments to the Claims:

Claim 1 (Previously Presented): An isolated or recombinant nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of:

- (a) a nucleotide sequence as shown in SEQ ID No.1;
- (b) a nucleotide sequence which is the complement of SEQ ID No.1;
- (c) a nucleotide sequence which is degenerate with SEQ ID No.1;
- (d) a nucleotide sequence hybridising under conditions of high stringency to (a), (b) or (c) or to a hybridisation probe derived from SEQ ID No.1 or the complement thereof;
- (e) a nucleotide sequence having at least 80% sequence identity with SEQ ID No.1; and
- (f) a fragment of (a), (b), (c), (d) or (e) above which is at least 10 nucleotides in length.

Claim 2 (Previously Presented): The nucleic acid according to claim 1 which encodes a polypeptide encoded by an open reading frame of a borrelidin biosynthetic gene cluster, or at least one domain thereof, wherein said polypeptide has an amino acid sequence selected from the group consisting of SEQ ID Nos.2 to 43 and 113, or at least 80% identity thereto.

Claim 3 (Previously Presented): The nucleic acid according to claim 2 comprising a sequence that encodes a PKS domain selected from AT0 and ACP0, said domains being described by, respectively, amino acids 322-664 and 694-763 of SEQ ID No.2.

Claim 4 (Previously Presented): The nucleic acid according to claim 3 comprising a sequence selected from the group consisting of bases 17147-18175 and 18263-18472 of SEQ ID No.1.

Claim 5 (Previously Presented): The nucleic acid according to claim 2 comprising a sequence that encodes a PKS domain

selected from KS1, AT1, KR1 and ACP1, said domains being described by, respectively, amino acids 34-459, 557-885, 1136-1379 and 1419-1486 of SEQ ID No.3.

Claim 6 (Previously Presented): A The nucleic acid according to claim 5 comprising a sequence selected from the group consisting of bases 18974-20251, 20543-21529, 22280-23011 and 23129-23332 of SEQ ID No.1.

Claim 7 (Previously Presented): The nucleic acid according to claim 2 comprising a sequence that encodes a PKS domain selected from KS2, AT2, DH2, KR2, ACP2, KS3, AT3, DH3, KR3 and ACP3, said domains being described by, respectively, amino acids 34-459, 559-887, 903-1050, 1354-1597, 1628-1694, 1724-2149, 2245-2576, 2593-2734, 3060-3307 and 3340-3406 of SEQ ID No.4.

Claim 8 (Previously Presented): The nucleic acid according to claim 7 comprising a sequence selected from the group consisting of bases 23785-25062, 25360-26346, 26392-26835, 27745-28476, 28567-28767, 28855-30132, 30418-31413, 31462-31887, 32863-33606 and 33703-33903 of SEQ ID No.1.

Claim 9 (Previously Presented): The nucleic acid according to claim 2 comprising a sequence that encodes a PKS domain selected from KS4, AT4, KR4 and ACP4, said domains being described by, respectively, amino acids 34-459, 555-886, 1179-1423 and 1459-1525 of SEQ ID No.5.

Claim 10 (Previously Presented): The nucleic acid according to claim 9 comprising a sequence selected from the group consisting of bases 34284-35561, 35847-36842, 37719-38453 and 38559-38759 of SEQ ID No.1.

Claim 11 (Previously Presented): The nucleic acid according to claim 2 comprising a sequence that encodes a PKS domain

selected from KS5, AT5, DH5, ER5, KR5 and ACP5, said domains being described by, respectively, amino acids 34-457, 553-888, 905-1046, 1401-1690, 1696-1942 and 1975-2041 of SEQ ID No.6.

Claim 12 (Previously Presented): The nucleic acid according to claim 11 comprising a sequence selected from the group consisting of bases 39221-40492, 40778-41785, 41834-42259, 43322-44191, 44207-44947 and 45044-45244 of SEQ ID No.1.

Claim 13 (Previously Presented): The nucleic acid according to claim 2 comprising a sequence that encodes a PKS domain selected from KS6, AT6, KR6, ACP6 and TE, said domains being described by, respectively, amino acids 37-457, 555-883, 1101-1335, 1371-1437 and 1461-1708 of SEQ ID No.7.

Claim 14 (Previously Presented): The nucleic acid according to claim 13 comprising a sequence selected from the group consisting of bases 45622-46884, 47176-48162, 48814-49518, 49624-49824 and 49894-50637 of SEQ ID No.1.

Claim 15 (Previously Presented): The nucleic acid according to claim 2 comprising a sequence that encodes a PKS module, said module being selected from the group consisting of amino acids 322-763 of SEQ ID No.2, 34-1486 of SEQ ID No.3, 34-1694 of SEQ ID No.4, 1724-3406 of SEQ ID No.4, 34-1525 of SEQ ID No.5, 34-2041 of SEQ ID No.6 and 37-1437 or 1708 of SEQ ID No.7.

Claim 16 (Previously Presented): The nucleic acid according to claim 15 comprising a sequence selected from the group consisting of bases 17147-18472, 18974-23332, 23785-28767, 28855-33903, 34284-38759, 39221-45244, 45622-49824 or 50637 of SEQ ID No.1.

Claim 17 (Previously Presented): The isolated or recombinant nucleic acid according to claim 1 wherein said nucleic acid sequence is selected from the group of genes consisting of:

borA1 (16184-18814 of SEQ ID NO: 1), *borA2* (18875-23590 of SEQ ID NO: 1), *borA3* (23686-34188 of SEQ ID NO: 1), *borA4* (34185-39047 of SEQ ID NO: 1), *borA5* (39122-45514 of SEQ ID NO: 1), *borA6* (45514-50742 of SEQ ID NO: 1), *borB* (7603-8397 of the complement strand of SEQ ID NO: 1), *borC* (8397-9194 of the complement strand of SEQ ID NO: 1), *borD* (9244-9996 of the complement strand of SEQ ID NO: 1), *borE* (9993-11165 of the complement strand of SEQ ID NO: 1), *borF* (11162-11980 of the complement strand of SEQ ID NO: 1), *borG* (11992-13611 of the complement strand of SEQ ID NO: 1), *borH* (13608-15659 of the complement strand of SEQ ID NO: 1), *borI* (50739-52019 of SEQ ID NO: 1), *borJ* (52113-53477 of SEQ ID NO: 1), *borK* (53486-54466 of SEQ ID NO: 1), *borL* (54506-56176 of SEQ ID NO: 1), *borM* (56181-57098 of SEQ ID NO: 1), *borN* (57112-57858 of SEQ ID NO: 1), *borO* (57939-59966 of SEQ ID NO: 1), *orfb1* (2-313 of SEQ ID NO: 1), *orfb2* (501-3107 of SEQ ID NO: 1), *orfb3* (3172-3810 of the complement strand of SEQ ID NO: 1), *orfb4* (3935-4924 of the complement strand of SEQ ID NO: 1), *orfb5* (5123-5953 of SEQ ID NO: 1), *orfb6* (5961-6518 of the complement strand of SEQ ID NO: 1), *orfb7* (6564-7538 of SEQ ID NO: 1), *orfb8* (60153-60533 of the complement strand of SEQ ID NO: 1), *orfb9* (60620-61003 of SEQ ID NO: 1), *orfb10* (61188-61436 of SEQ ID NO: 1), *orfb11* (61526-61738 of SEQ ID NO: 1), *orfb12* (61767-62285 of the complement strand of SEQ ID NO: 1), *orfb13a* (62750-63067 of the complement strand of SEQ ID NO: 1), *orfb13b* (62586-62858 of the complement strand of SEQ ID NO: 1), *orfb14* (63155-65071 of the complement strand of SEQ ID NO: 1), *orfb15* (65374-65871 of SEQ ID NO: 1), *orfb16* (65942-68305 of the complement strand of SEQ ID NO: 1), *orfb17* (68290-68910 of the complement strand of SEQ ID NO: 1), *orfb18* (69681-70436 of SEQ ID NO: 1), *orfb19* (70445-71848 of SEQ ID NO: 1), *orfb20* (71851-72957 of SEQ ID NO: 1), *orfb21* (73037-73942 of SEQ ID NO: 1) and *orfb22* (73995-74534 of the complement strand of SEQ ID NO: 1).

Claim 18 (Previously Presented): An isolated polypeptide encoded by the nucleic acid sequence of claim 1.

Claim 19 (Previously Presented): A method of modifying a parent polyketide synthase, comprising introducing into a host cell the nucleic acid molecule of claim 1, wherein said nucleic acid molecule encodes a domain from a borrelidin polyketide synthase, or a derivative thereof, wherein the host cell contains nucleic acid encoding said parent polyketide synthase, such that, when expressed, the domain is incorporated into said parent polyketide synthase.

Claim 20 (Previously Presented): The method according to claim 19 wherein the borrelidin PKS domain is inserted in addition to the native domains of the parent PKS.

Claim 21 (Previously Presented): The method according to claim 19 wherein the borrelidin PKS domain is inserted in place of a native domain of the parent PKS.

Claim 22 (Previously Presented): The method according to claim 21 wherein a domain of the parent polyketide synthase is inactivated, deleted or altered.

Claim 23 (Previously Presented): The method according to claim 19 comprising introducing a nucleic acid encoding a module from said borrelidin polyketide synthase, or a derivative thereof, into said host cell.

Claim 24 (Previously Presented): The method according to claim 23 wherein said module is an extender module comprising at least ACP, AT and KS domains.

Claim 25 (Previously Presented): The method according to claim 24 wherein said module further comprises a KR domain.

Claim 26 (Previously Presented): The method according to claim 25 wherein said module further comprises a DH domain.

Claim 27 (Previously Presented): The method according to claim 26 wherein said module further comprises an ER domain.

Claim 28 (Previously Presented): The method according to claim 24 wherein said module further comprises a TE domain.

Claim 29 (Original): A method of modifying a parent borrelidin polyketide synthase comprising introducing into a host cell a nucleic acid encoding a domain from a donor polyketide synthase, wherein the host cell contains nucleic acid encoding said parent borrelidin polyketide synthase, such that, when expressed, the domain is incorporated into said parent borrelidin polyketide synthase.

Claim 30 (Previously Presented): The method according to claim 29 wherein the donor PKS domain is inserted in addition to the native domains of the parent borrelidin PKS.

Claim 31 (Previously Presented): The method according to claim 29 wherein the donor PKS domain is inserted in place of a native domain of the parent borrelidin PKS.

Claim 32 (Previously Presented): The method according to claim 29 wherein the donor PKS domain is selected from the group consisting of O-methyl transferase domains, C-methyl transferase domains, epimerisation domains, monooxygenase domains, dehydrogenase domains, aminotransferase domains or non-ribosomal peptide synthetase domains.

Claim 33 (Previously Presented): The method according to claim 29 comprising introducing a nucleic acid encoding a module from said donor polyketide synthase, or a derivative thereof, into said host cell.

Claim 34 (Previously Presented): The method according to claim 33 wherein said module is an extender module comprising at least ACP, AT and KS domains.

Claim 35 (Previously Presented): The method according to claim 34 wherein said module further comprises a KR domain.

Claim 36 (Previously Presented): The method according to claim 35 wherein said module further comprises a DH domain.

Claim 37 (Previously Presented): The method according to claim 36 wherein said module further comprises an ER domain.

Claim 38 (Previously Presented): The method according to claim 33 wherein said module further comprises a TE domain.

Claim 39 (Previously Presented): The method according to claim 29 wherein the donor PKS is a borrelidin PKS.

Claim 40 (Previously Presented): A nucleic acid construct comprising at least one first nucleic acid portion which is the nucleic acid molecule of claim 1, wherein said at least one first nucleic acid portion encodes at least one domain of a borrelidin PKS and a second nucleic acid portion or portions encoding at least one type I PKS domain which is heterologous to said borrelidin PKS.

Claim 41 (Previously Presented): The construct according to claim 40 comprising a hybrid polyketide synthase gene, said gene encoding at least one domain of a borrelidin PKS and at least one type I PKS domain which is heterologous to said borrelidin PKS.

Claim 42 (Previously Presented): The method of claim 74 comprising upregulating a borrelidin biosynthetic gene

involved in production of the borrelidin starter unit in said cell.

Claim 43 (Previously Presented): The method according to claim 42 wherein said gene is selected from the group consisting of *borC*, *borD*, *borE*, *borF*, *borH*, *borK*, *borL*, *borM* and *borN*.

Claim 44 (Previously Presented): The method according to claim 43 wherein the gene is *borE* or *borL*.

Claim 45 (Previously Presented): The method according to claim 42 comprising the step of introducing a nucleic acid encoding the gene to be upregulated into said cell.

Claim 46 (Previously Presented): The method of claim 74 comprising deleting, disrupting, or otherwise inactivating a borrelidin biosynthetic gene involved in production of the borrelidin starter unit in said cell, wherein the gene is *borG*.

Claim 47 (Previously Presented): The method according to claim 46 comprising fermenting the resulting cell and feeding an exogenous carboxylic acid.

Claim 48 (Previously Presented): The method of claim 47, wherein the exogenous carboxylic acid is selected from the group consisting of *trans*-cyclobutane-1,2-dicarboxylic acid, 2,3-dimethylsuccinic acid, 2-methylsuccinic acid, and *trans*-cyclopentane-1,2-dicarboxylic acid.

Claim 49 (Previously Presented): The method of claim 46, wherein the method additionally comprises deleting, modifying or replacing one or more borrelidin biosynthetic genes, or borrelidin polyketide synthase domains or modules.

Claim 50 (Previously Presented): A method for producing a

modified borrelidin polyketide or derivative thereof in a host cell expressing a PKS for borrelidin or a derivative thereof, the method comprising the deletion or inactivation of at least one gene responsible for the formation of the nitrile function at C12 of borrelidin.

Claim 51 (Previously Presented): The method according to claim 50 comprising the introduction into said host cell of nucleic acid encoding at least one heterologous genes to allow alternative elaboration of any accumulated biosynthetic intermediates or shunt metabolites.

Claim 52 (Previously Presented): A vector which comprises a nucleic acid molecule as defined in claim 1.

Claim 53 (Original): A host cell comprising the vector of claim 52.

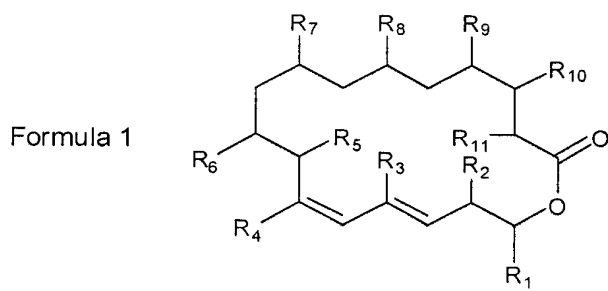
Claim 54 (Original): The host cell of claim 53, wherein the host cell is an Actinomycete.

Claim 55 (Original): The host cell of claim 53, wherein the host cell is a Streptomyces.

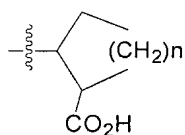
Claim 56 (Original): The host cell of claim 55, wherein the host cell is selected from the group consisting of *Saccharopolyspora erythraea*, *Streptomyces coelicolor*, *Streptomyces avermitilis*, *Streptomyces griseofuscus*, *Streptomyces cinnamonensis*, *Micromonospora griseorubida*, *Streptomyces hygroscopicus*, *Streptomyces fradiae*, *Streptomyces longisporoflavus*, *Streptomyces lasaliensis*, *Streptomyces tsukubaensis*, *Streptomyces griseus*, *Streptomyces venezuelae*, *Streptomyces antibioticus*, *Streptomyces lividans*, *Streptomyces rimosus* and *Streptomyces albus*. *Streptomyces rochei* ATCC23956, *Streptomyces parvulus* Tü113.

Claim 57 (Previously Presented): A method for the synthesis of polyketides comprising culturing the host cell of claim 53.

Claim 58 (Previously Presented): The compound of claim 75, or a pharmaceutically acceptable salt thereof, said compound having the formula:



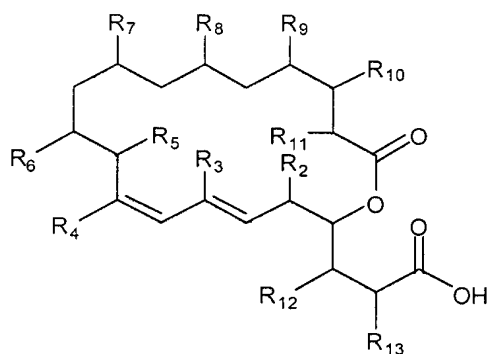
wherein R₁ is a cycloalkyl group of the formula, n being 1-2



and R₁ can also optionally be substituted with at least one halo atom or at least one C₁ to C₃ alkyl group; R₂, R₃, R₆, R₇, R₈, R₉, or R₁₁ are each independently H, OCH₃, CH₃ or CH₂CH₃; R₄ is CN, CO₂H, CHO, CH₃, CONH₂, CHNH; R₅, R₁₀ are OH; or analogues differing from the corresponding "natural" compound in the oxidation state of one or more of the ketide units, with the proviso that said compounds are not borrelidin (**1**), 12-desnitrile-12-carboxyl borrelidin (**2**), 10-desmethyl borrelidin (**3**), 11-epiborrelidin (**4**) or C14,C15-*cis* borrelidin analogue (**5**) as shown in Figure 1.

Claim 59 (Previously Presented): The compound of claim 75, or a pharmaceutically acceptable salt thereof, said compound having the formula:

Formula 2



wherein R₂, R₃, R₆, R₇, R₈, R₉, or R₁₁ are each independently H, OCH₃, CH₃ or CH₂CH₃; R₄ is CN, CO₂H, CHO, CH₃, CONH₂, CHNH, R₅, R₁₀ are OH; or analogues differing from the corresponding natural compound in the oxidation state of one or more of the ketide units (i.e. selection of alternatives from the group: -CO-, -CH(OH)-, =CH-, and -CH₂-), and R₁₂ and R₁₃ are independently H or a C1-C4 alkyl group which may be optionally substituted with OH, F, Cl, SH) with the proviso that R₁₂ and R₁₃ are not simultaneously H.

Claim 60 (Previously Presented): The compound or salt according to claim 75, wherein R₇, R₈ and R₉ of formulas 1 and 2 are all CH₃.

Claim 61 (Previously Presented): The compound or salt according to claim 75, wherein R₄ of formulas 1 and 2 is CH₃ or COOH.

Claim 62 (Previously Presented): The compound or salt according to claim 60 wherein R₄ of formulas 1 and 2 is CH₃ or COOH.

Claim 63 (Previously Presented): The compound or salt according to claim 75, wherein R₄ of formulas 1 and 2 is CN.

Claim 64 (Previously Presented): The compound or salt according to claim 60 wherein R₄ of formulas 1 and 2 is CN.

Claim 65 (Previously Presented): The compound or salt according to claim 58 wherein R₁ is cyclobutane-1'-carboxylate.

Claim 66 (Previously Presented): The compound or salt according to claim 60, wherein R₁ of formula 1 is cyclobutane-1'-carboxylate.

Claim 67 (Previously Presented): The compound or salt according to claim 66, wherein R₄ of formulas 1 and 2 is CH₃ or COOH.

Claim 68 (Previously Presented): The compound or salt according to claim 58, wherein R₆, R₇, R₈ and R₉ are all CH₃, R₂ and R₁₁ are H, R₅ and R₁₀ are OH, R₄ is either CH₃, COOH or CN and R₁ is cyclopentane-1'-carboxylate or cyclobutane-1'-carboxylate.

Claim 69 (Previously Presented): The compound or salt according to claim 59, wherein R₁₂ and R₁₃ are independently CH₃ or H.

Claim 70 (Previously Presented): The compound or salt according to claim 60, wherein R₁₂ and R₁₃ of formula 2 are independently CH₃ or H.

Claim 71 (Previously Presented): The compound or salt according to claim 70, wherein R₄ of formulas 1 and 2 is CH₃ or COOH.

Claim 72 (Previously Presented): The compound or salt according to claim 59 wherein R₆, R₇, R₈ and R₉ are all CH₃, R₂ and R₁₁ are H, R₅ and R₁₀ are OH, R₄ is either CH₃, COOH or CN and R₁₂ and R₁₃ are independently CH₃ or H.

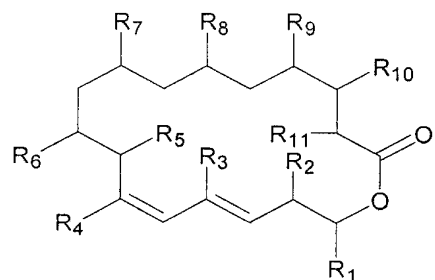
Claim 73 (Previously Presented): The compound or salt

according to claim 59 wherein R_6 , R_7 , R_8 and R_9 are all CH_3 , R_2 and R_{11} are H , R_5 and R_{10} are OH , R_4 is either CH_3 , COOH or CN and R_{12} and R_{13} are both CH_3 .

Claim 74 (Previously Presented): A method for increasing the capacity of a host cell to produce borrelidin, or a borrelidin derivative or analogue in a host cell expressing a polyketide synthase, said method selected from the group consisting of:

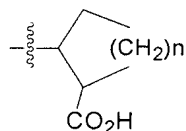
- a) a method comprising upregulating a borrelidin biosynthetic gene involved in production of the borrelidin starter unit in said cell; and
- b) a method comprising deleting, disrupting, or otherwise inactivating a borrelidin biosynthetic gene involved in production of the borrelidin starter unit in said cell, wherein the gene is *borG*.

Claim 75 (Previously Presented): A compound, said compound being selected from the group consisting of formula 1,



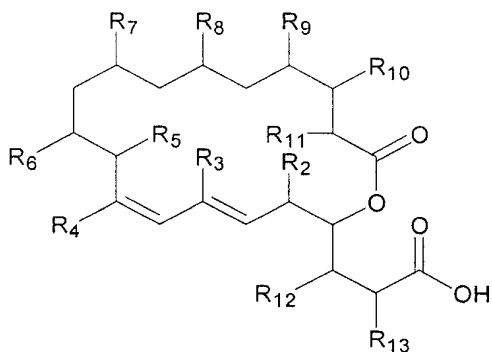
, and pharmaceutically acceptable salts thereof, wherein

R_1 is a cycloalkyl group of the formula, n being 1- 2,



and R_1 can also optionally be substituted with at least one halo atoms or at least one C_1 to C_3 alkyl groups; R_2 , R_3 , R_6 , R_7 , R_8 , R_9 , or R_{11} are each independently H , OCH_3 , CH_3 or CH_2CH_3 ; R_4 is CN , CO_2H , CHO , CH_3 , CONH_2 , CHNH ; R_5 , R_{10} are OH ; or analogues differing from the corresponding "natural" compound in the oxidation state of one or more of the ketide units (i.e. selection of alternatives from the group: $-\text{CO}-$, $-\text{CH}(\text{OH})-$

, =CH-, and -CH₂-), with the proviso that said compounds are not borrelidin (**1**), 12-desnitrile-12-carboxyl borrelidin (**2**), 10-desmethyl borrelidin (**3**), 11-epiborrelidin (**4**) or C14,C15-*cis* borrelidin analogue (**5**) as shown in Figure 1; and formula



, wherein R₂, R₃, R₆, R₇, R₈, R₉, or R₁₁ are each independently H, OCH₃, CH₃ or CH₂CH₃; R₄ is CN, CO₂H, CHO, CH₃, CONH₂, CHNH, R₅, R₁₀ are OH; or analogues differing from the corresponding natural compound in the oxidation state of one or more of the ketide units, and R₁₂ and R₁₃ are independently H or a C1-C4 alkyl group which may be optionally substituted with OH, F, Cl, SH) with the proviso that R₁₂ and R₁₃ are not simultaneously H.

Claim 76 (Previously Presented): A vector which comprises a nucleic acid construct as defined in claim 40.

Claim 77 (Previously Presented): A host cell comprising the vector of claim 76.

Claim 78 (Previously Presented): The host cell of claim 77, wherein the host cell is an Actinomycete.

Claim 79 (Previously Presented): The host cell of claim 77, wherein the host cell is a Streptomyces.

Claim 80 (Previously Presented): The host cell of claim 79, wherein the host cell is selected from the group consisting of *Saccharopolyspora erythraea*, *Streptomyces coelicolor*, *Streptomyces avermitilis*, *Streptomyces griseofuscus*,

Streptomyces cinnamomensis, *Micromonospora griseorubida*, *Streptomyces hygroscopicus*, *Streptomyces fradiae*, *Streptomyces longisporoflavus*, *Streptomyces lasaliensis*, *Streptomyces tsukubaensis*, *Streptomyces griseus*, *Streptomyces venezuelae*, *Streptomyces antibioticus*, *Streptomyces lividans*, *Streptomyces rimosus* and *Streptomyces albus*. *Streptomyces rochei* ATCC23956, *Streptomyces parvulus* Tü113.

Claim 81 (Previously Presented): A method for the synthesis of polyketides comprising culturing the host cell of claim 77.

Claim 82 (Currently Amended): A method for modifying a host cell to increase its capacity for the production of borrelidin, or a borrelidin derivative or analogue, the host cell being capable of expressing a polyketide synthase for borrelidin or said derivative or analogue, the method comprising deleting, disrupting, or otherwise inactivating a borrelidin biosynthetic gene involved in production of the borrelidin starter unit in said cell, wherein the gene is selected from the list consisting of *borC*, *borD*, *borE*, *borF*, *borG*, *borH*, *borK*, *borL*, *borM* and \pm *borN*.

Claim 83 (Previously Presented): The method according to claim 82 wherein the gene is *borG*.

Claim 84 (Previously Presented): The method according to claim 82 wherein the gene is *borE*.

Claim 85 (Previously Presented): The method according to claim 82 comprising fermenting the resultant cell and feeding an exogenous carboxylic acid.

Claim 86 (Previously Presented): The method of claim 82 wherein the gene is *borG* and the exogenous carboxylic acid is selected from the group consisting of trans-cyclobutane-1,2-dicarboxylic acid, 2,3-dimethylsuccinic acid, 2-methylsuccinic

acid, and trans-cyclopentane-1,2-dicarboxylic acid.

Claim 87 (Previously Presented): The method of claim 82, wherein the gene is *borG* and the method additionally comprises deleting, modifying or replacing one or more borrelidin biosynthesis genes or borrelidin polyketide synthase domains or modules.

Claim 88 (Previously Presented): A host cell capable of expressing a polyketide synthase for borrelidin or a borrelidin derivative or analogue, in which a borrelidin biosynthetic gene involved in production of the borrelidin starter unit in said cell, has been deleted, disrupted, or otherwise inactivated wherein said gene is selected from the list consisting of *borC*, *borD*, *borE*, *borF*, *borG*, *borH*, *borK*, *borL*, *borM* and *borN*.

Claim 89 (Previously Presented): The host cell according to claim 88 wherein the gene is *borG*.

Claim 90 (Previously Presented): The host cell according to claim 89 in which one or more borrelidin biosynthesis genes or borrelidin polyketide synthase domains or modules are additionally deleted, modified or replaced.

Claim 91 (Previously Presented): The host cell according to claim 88 which is an Actinomycete.

Claim 92 (Previously Presented): The host cell according to claim 88 which is a Streptomyces.

Claim 93 (Previously Presented): The host cell according to claim 88 wherein the host cell is selected from the group consisting of *Saccharopolyspora erythraea*, *Streptomyces coelicolor*, *Streptomyces avermitilis*, *Streptomyces griseofuscus*, *Streptomyces cinnamonensis*, *Micromonospora*

griseorubida, *Streptomyces hygroscopicus*, *Streptomyces fradiae*, *Streptomyces longisporoflavus*, *Streptomyces lasaliensis*, *Streptomyces tsukubaensis*, *Streptomyces griseus*, *Streptomyces venezuelae*, *Streptomyces antibioticus*, *Streptomyces lividans*, *Streptomyces rimosus*, *Streptomyces albus*, *Streptomyces rochei* ATCC23956, *Streptomyces parvulus* Tü113, and *Streptomyces parvulus* Tü4055.

Claim 94 (Previously Presented): A method for producing of borrelidin, or a borrelidin derivative or analogue, said method comprising fermenting a host cell according to claim 88 and feeding an exogenous carboxylic acid.

Claim 95 (Previously Presented): The method of claim 94 wherein the gene is *borG* and wherein the exogenous carboxylic acid is selected from the group consisting of trans-cyclobutane-1,2-dicarboxylic acid, 2,3-dimethylsuccinic acid, 2-methylsuccinic acid, and trans-cyclopentane-1,2-dicarboxylic acid.